Pathologic Fracture Occurring 22 Years After Diagnosis of Hairy Cell Leukemia: Case Report and Literature Review

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HAIRY CELL LEUKEMIA (HCL) is a chronic B-cell lymphoproliferative disorder that accounts for approximately 2% of all leukemias.[1,2] The typical clinical picture consists of a man with a median age of between 50 and 55 years with splenomegaly, a varying degree of pancytopenia without lymphadenopathy, and characteristic hairy cells in peripheral blood and bone marrow.[1,2] Bone lesions, having an incidence of 3%, are an uncommon complication of HCL.[1,3] We present a patient who developed a pathologic fracture 22 years after his initial diagnosis. We also provide a review of the literature on this rare complication of HCL.

Case Report

The patient is a 67-year-old man first diagnosed with HCL in November 1973. He underwent splenectomy in January 1974, and was treated with single-agent, chlorambucil therapy from November 1979 to February 1981. His HCL therapy was reinitiated in April 1988, with interferon alpha-2b and was discontinued in July 1989, after achieving an impressive partial response in the abdominal lymph nodes on computed tomographic (CT) scan. Evidence of recurrent disease in the abdominal lymph nodes led to the reinitiation of interferon alpha-2b therapy in December 1990. This therapy was continued until December 1992, when the patient made an informed decision to discontinue the interferon alpha-2b therapy, despite having achieved another partial response in the abdominal lymph nodes.

On July 1 1996, while working on his lawnmower, the patient noted a severe, sharp, stabbing pain in the right proximal leg. The pain started just above the knee and spread to involve the area between the groin and the knee. The patient went to his primary care physician and was referred to a neurologist, who diagnosed a painful mononeuropathy. The patient developed proximal leg weakness and swelling of the right leg and foot over the ensuing month. On July 12, 1996, a CT scan of the chest, abdomen, and pelvis showed no changes to suggest progressive HCL. Laboratory evaluation on July 16, 1996, showed a normal serum calcium of 2.35 mmol/liter (reference: 2.15–2.50 mmol/liter) and a normal serum-alkaline phosphatase of 72 U/liter (reference: less than 250 U/liter).

On August 1, 1996, the patient was sent to the University of South Alabama Medical Center for oncologic evaluation. On physical examination, the patient's right leg was extremely tender to palpation, particularly in the area of the proximal femur. The range of motion of the right hip joint was severely limited by pain. The patient was unable to bear weight on his right leg. No peripheral lymphadenopathy was noted on examination. Anteroposterior radiograph of the right pelvis and femur (Figure 1) showed shortening of the neck of the femur with overlap, which is consistent with a femoral neck fracture. A cemented bipolar arthroplasty was subsequently performed on the right hip. At the time of surgery, the greater trochanter was found to be separated from the femoral neck. The proximal femur was noted to be grossly tumorous. A large mass was removed from the proximal femur and greater trochanter. Pathologic evaluation of the specimen found a leukemic infiltrate completely filling the marrow space in the femoral head and present in fragments of the femoral neck. The leukemic infiltrate abutted thinned, bony trabeculae and areas of necrosis (Figure 2). Flow cytometry studies revealed a monoclonal, B-cell population positive for HLA-DR, CD45, CD19, CD20, CD22, and, most significantly, CD11c and CD25. The population showed kappa light chain restriction. The leukemic infiltrate also had the cytologic features of HCL. Immunohistochemical stains for acid phosphatase and for tartrate-resistant acid phosphatase were positive on the tumor cells.

The patient received no further treatment and recovered without further complications. A bone scan in November 1997 showed no abnormalities aside from the patient's right hip replacement. As of June 1997, the patient continued to do well, with no further complaint of bony pain and no further treatment for his HCL as of that time.

Discussion

We found 32 patients with bony complications of HCL reported in the English literature,[3-17] as well as others reported in the non-English literature.[18-21] The frequency of these complications is reported to be between 0%[22] and 13%.[9] The largest case study reported an incidence of 3%, or in 8 of 267 HCL patients.[3] In contrast, multiple myeloma has a bone lesion frequency of 79%,[23] and other malignant lymphomas have an intermediate frequency of about 27%.[24] The first 3 documented cases of osteolytic bone lesions in HCL patients were presented in 1977.[4] These patients had been diagnosed with HCL two to three years prior to the publication of the report, and two out of the three patients had lesions located in the femoral neck region. The interval between diagnosis of HCL and develop-

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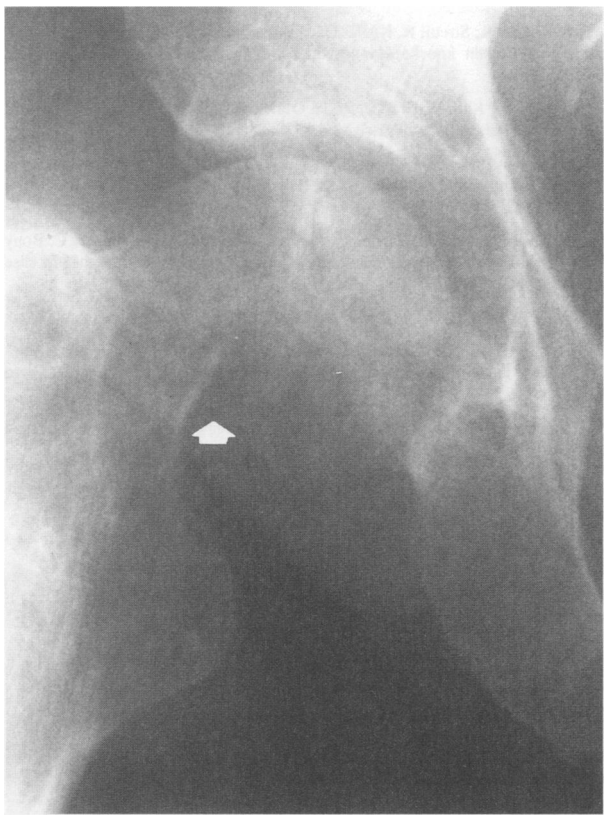

Figure 1.—This anteroposterior radiograph of the right proximal femur demonstrates a shortening and angulation (white arrow) of the neck of the femur with overlap consistent with a femoral neck fracture.

ment of bony lesions can vary greatly. The lesion can be the initial symptom of HCL[3,7,11,16,17] or may not present for up to 73 months.[3] Our patient presented 22 years after his diagnosis, which is the longest documented interval between a diagnosis of HCL and the development of a bone lesion. This case demonstrates the need for diligent long-term follow-up of cancer patients by their primary care physicians. Localized pain is common to all documented cases, but the pain may precede skeletal roentgenographic abnormalities.[5,6,8,14,17] Laboratory evaluation of the documented patients revealed normal serum calcium and alkaline phosphatase levels, and the same results were obtained in the case we are presenting. A few documented cases have reported alkaline phosphatase elevations associated with the liver instead of bone.[4,7,8,14]

The HCL-associated bony lesions have a predilection for the axial skeleton, with the femoral head, neck, or both accounting for 24 in 31, or about 77% of the cases. This also holds true for the case we are presenting. Other sites include the skull, vertebrae, ribs, humerus, pelvis, tibia, and fibula. As in the present case, the right side is predominantly affected by the lesions. Reported skeletal roentgenographic abnormalities occurred in five different patterns. The predominant pattern is that of an osteolytic lesion occurring in about 77% of the cases (24 of 31).

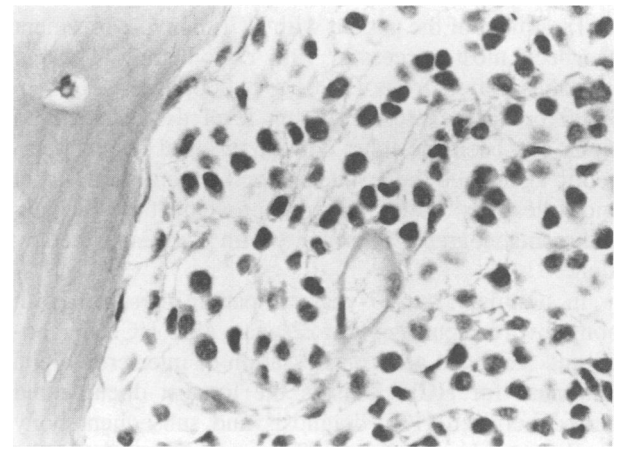

Figure 2.—A medium-high-power view of the femoral neck shows marrow space (adjacent to a bony trabeculae) completely replaced with a uniform population of cells. These cells have nuclei slightly larger than mature lymphocytes and delicate, "feathery" cytoplasm. These are the "hairy cells."

The lesions can present with either well-defined or poorly-defined margins. Diffuse demineralization of the bone is the next most common pattern, reported in 5 of 31 cases.[9,14,17,18] The demineralization can be widespread, local, or associated with an osteolytic lesion. Demeter and colleagues[17] presented two patients complaining of bone pain, both of whom had demineralization lesions and overall decreased bone density. Osteosclerosis occurs infrequently—only four cases have been reported—and presents in a diffuse pattern.[14,16,18] Hudson and colleagues[18] reported an increased bone density associated with the osteosclerotic lesion. Isolated necrosis of the femoral head has been reported in three cases and was the direct cause of a fracture in two of the cases.[3,9,17] Osteoblastic lesions occur least frequently; there are only two reported cases.[7,14] In both cases, the lesion was focally osteolytic, creating a mixed pattern.

In all reported cases, no cortical bone destruction or periosteal reaction was documented. Marcelli and colleagues[15] did report abnormal bone remodeling and a significant increase in bone resorption in three cases.

In the evaluation of bone pain, skeletal roentgenographic studies are the most commonly used technique. Bone scans have been reported to be very effective in supporting roentgenographic findings and have been reported to document lesions when roentgenographic studies were normal.[3,16,23] A positive bone scan shows increased, radionuclide uptake in the area of bony involvement. Magnetic resonance imaging (MRI) scans with T1-weighted images have been used increasingly to confirm lesions found on both roentgenographs and bone scans.[13,14] The MRI scans show non-homogeneous decreases in signal intensity, which are interpreted as hairy-cell infiltration. In the future MRI scans may be used to evaluate further those patients who have multiple areas of bone pain and normal-appearing roentgenographs.

Treatment of the patient with HCL bony involvement has been most successful with radiotherapy. The rad level has varied from 1,500[3] to 6,000,[4] with 2,000 to 3,000 being the most common level used. Interferon alpha has been the most commonly used chemotherapeutic agent, and the results are well documented. Arkel and colleagues[10] also reported improvement in bone pain and roentgenograph abnormality with prednisone therapy alone.

In summary, our 67-year-old patient presented with bony involvement by HCL 22 years after HCL diagnosis and 3.5 years after his cessation of interferon-alpha treatment for HCL. This is the longest documented period between HCL diagnosis and subsequent bony involvement by the disease. This case demonstrates the need for diligent, long-term observation of HCL patients by primary care physicians and other health care professionals. Any complaint of bone pain by a patient with a hematological cancer should be evaluated fully with radiographic methods.

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Endotracheal Intubation and Mechanical Ventilation Following Respiratory Arrest From High Altitude Pulmonary Edema

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High altitude pulmonary edema (HAPE) is a severe form of altitude illness occurring in some inadequately acclimatized individuals as a result of rapid ascent to high altitude. HAPE is a noncardiogenic pulmonary edema that may be rapidly fatal and can occur with or without prodromal symptoms. Fast recovery is common, however, with early recognition and descent to a lower altitude.[1]

Endotracheal intubation and mechanical ventilation are indicated in a variety of pulmonary, cardiovascular, and neurologic disorders to optimize ventilation and oxygenation as well as protect the airway.[2] The role of prehospital intubation in the management of severe HAPE has not been previously discussed in the literature. This report presents a case of persistent HAPE that resulted in cardiopulmonary arrest following a 2,300 meter descent. The case was managed with endotracheal intubation and manual mechanical ventilation performed

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